

Lumbar spinal malignant peripheral nerve sheath tumor arising from a benign neurofibroma

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We present the case of a 27-year-old man who had a soft-tissue lumbar spine mass causing back, abdominal, and groin pain. Imaging showed the lesion filling the right neural foramen, invading the anterior L2 vertebral body and both pedicles, and protruding into the central canal, causing compression of the thecal sac. The final pathologic diagnosis was a malignant peripheral nerve sheath tumor, with histologic evidence of a precursor neurofibroma. The patient did not have an underlying diagnosis of neurofibromatosis.

Introduction

While neurofibromas are common benign masses of the spinal canal, malignant degeneration of neurofibromas is rarely seen, except in cases associated with neurofibromatosis (NF1) (1-3). We present a case of a lumbar spine malignant peripheral nerve sheath tumor (MPNST) arising from a benign neurofibroma in a patient without NF1.

Case report

A 27-year-old man presented to the Emergency Department with complaints of right lower quadrant abdominal pain of three days' duration, concerning for appendicitis. The pain was associated with pelvic pressure and groin pain that radiated down his right leg and was partially relieved with thigh flexion. His past medical history included progressively worsening back pain of three months' duration that he believed began after moving a heavy couch. On physical exam, he had right-lower-quadrant abdominal tenderness without peritoneal signs.

Abdominal radiographs showed no evidence of abdominal pathology but did show obscuration of the right L2 pedicle, suggesting a lumbar spinal mass (Fig. 1, arrow). CT examination excluded appendicitis and confirmed a large, destructive, lytic lesion of the L2 vertebral body and right pedicle (Fig. 2A, B). There was associated narrowing of the central spinal canal as well as loss of definition of the normal fatty tissue boundary between the right psoas muscle and the lumbar spine (Fig. 2C). The lesion itself was primarily isoattenuating to muscle. A small portion of the mass near the right L1-L2 neural foramen was hypoattenuating; it contained a central focus of higher attenuation, akin to a target sign (Fig. 2C, arrow). Magnetic resonance imaging (Fig. 3) further delineated an expansile soft-tissue mass diffusely invading the L2 vertebral body, filling the right L1-L2 neural foramen, and displacing the thecal sac posteriorly with near-complete obliteration of the CSF space. The mass was hypointense to normal bone marrow on T1-weighted sequences, hyperintense on T2-weighted sequences, and avidly enhanced following administration of gadolinium. The neuroforaminal portion of the mass demonstrated a target-like appearance on T2-weighted sequences, with a hyperintense halo surrounding a central hypointense region (Fig. 3, arrow).

CT-guided needle biopsy suggested a spindle-cell neoplasm. Metastatic workup was negative. Angiography demonstrated a hypervascular mass at L2, and pre-operative tumor embolization was performed using coils and Gel-foam (Fig. 4). The tumor was completely excised the next day, in conjunction with L2 corpectomy and L1-L3 laminectomies with posterior spinal fusion. At the time of surgery, dense retroperitoneal adhesions required extensive

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Figure 1. 27-year-old man with MPNST. Supine radiograph of the abdomen reveals mild height loss of the L2 lumbar vertebral body, with indistinctness of the right lateral border, and nonvisualization of the right pedicle (arrow). These signs indicate a destructive lumbar spinal mass.

tissue dissection, ultimately resulting in a left nephrectomy. Because the surgery was performed in several stages, the tumor was excised in multiple pieces and its exact size was difficult to determine.

H&E-stained sections revealed fragments of skeletal muscle, fibrovascular tissue and fat, peripheral nerve, and bone associated with a spindle-cell neoplasm with varying cytologic morphology. The lesion appeared microscopically to arise from a neurofibroma (Fig. 5). This benign neurofibroma however, transitioned through histologic phases of increasing cytologic atypia, cell density, nuclear pleomorphism, and mitotic activity to become, in most sections, a hypercellular spindle-cell lesion (Fig. 6) with moderate differentiation and up to 26 mitotic figures per 10 high-power fields. There was no definite tumor necrosis. Immunohistochemical stains were positive for CD99 and p75 (Fig. 7A), and negative for S-100, CD34, and C-kit (Fig. 7B). Several foci of malignant osteoid formation were evident on Gomori trichrome staining (Fig. 7C). The final pathologic diagnosis was MPNST arising from a precursor neurofibroma, with focal infiltration of fibroadipose tissue and skeletal muscle and local invasion of bone.

The patient's postoperative course was complicated by an acute pulmonary embolism, treated with Coumadin, and subsequently by the development of two large surgical-site hematomas. At last followup, there was no evidence for local recurrence or metastatic disease.

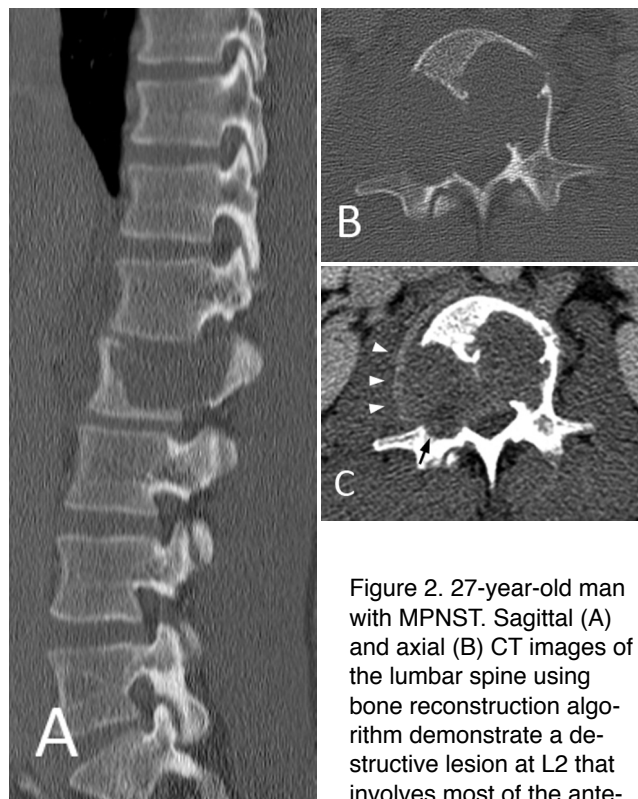


Figure 2. 27-year-old man with MPNST. Sagittal (A) and axial (B) CT images of the lumbar spine using bone reconstruction algorithm demonstrate a destructive lesion at L2 that involves most of the anterior vertebral body, both

pedicles, and the right lamina. Adjacent disc spaces are normal. (C) Axial contrast-enhanced CT image through L2 with soft-tissue reconstruction algorithm shows an expansile soft-tissue mass invading the anterior vertebral body and protruding posteriorly into the central canal, causing moderate central stenosis. There is loss of the normal fat plane between the spine and the right psoas muscle (white arrows). The lesion is primarily isoattenuating to muscle, and contains a small hypoattenuating round focus with central high attenuation (target sign, arrow).

Discussion

Complicated low back pain

The patient presented with abdominal pain. Since he also had severe back pain progressively worsening for twelve weeks, diagnostic imaging might have been initiated sooner. Although imaging is not indicated for the majority of cases of acute low back pain (4), the ACR recommends imaging in cases where there is significant concern for infection, tumor, fracture, or cauda equina syndrome (5). Clinical indicators include unexplained fever or weight loss, focal neurologic deficits, age greater than 70, and duration

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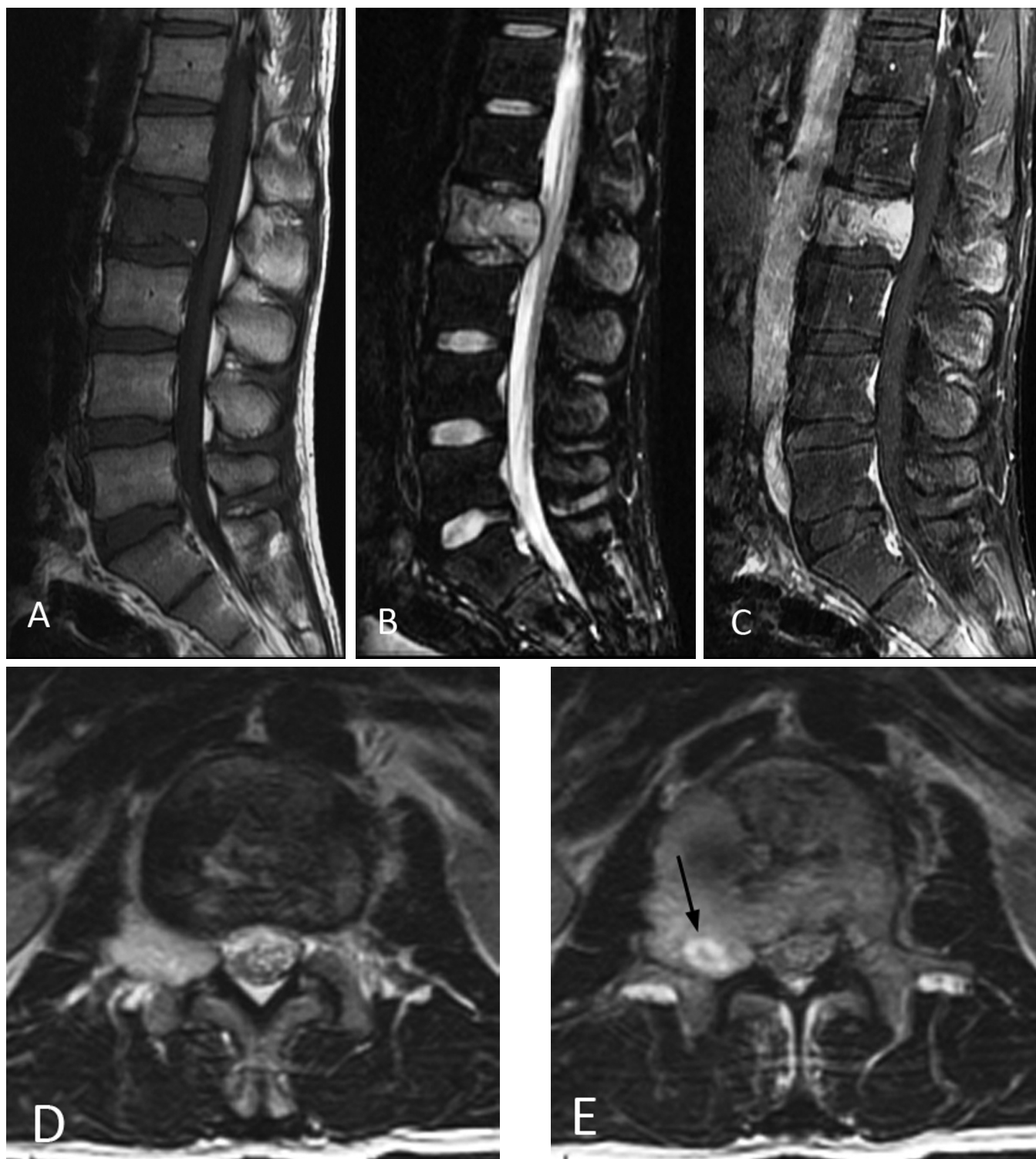


Figure 3A-E. 27-year-old man with MPNST. Sagittal T1-weighted (A), T2-weighted (B), and T1-weighted gadolinium-enhanced (C) MR images of the lumbar spine demonstrate a soft-tissue mass involving most of the L2 vertebral body. The mass is hypointense on T1, hyperintense on T2, and enhances with gadolinium. Sequential axial T2-weighted MR images through the mass (D, E) demonstrate soft tissue filling the right L1-L2 neural foramen, extending anteriorly to involve most of the L2 vertebral body and both pedicles, and protruding posteriorly to displace the thecal sac, with near-complete obliteration of the CSF space. Arrow in (E) indicates the "MRI target sign."

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longer than six weeks (see List of red flags, at end of article) (5). The presence of any such complicating features mandates an imaging workup, starting with lumbar spine radiographs, and often followed by MR imaging. In the case reported here, the imaging workup facilitated the diagnosis and treatment of a MPNST arising from a benign lumbar spinal neurofibroma.

Benign peripheral nerve sheath tumors

Neurofibromas are common benign fibroblastic neoplasms of peripheral-nerve-sheath origin that occur both sporadically as well as in NF1. Most neurofibromas occur sporadically, as solitary, localized tumors characterized by a fusiform shape with normal nerve entering and exiting on either side (3). Histologically, localized neurofibromas con-

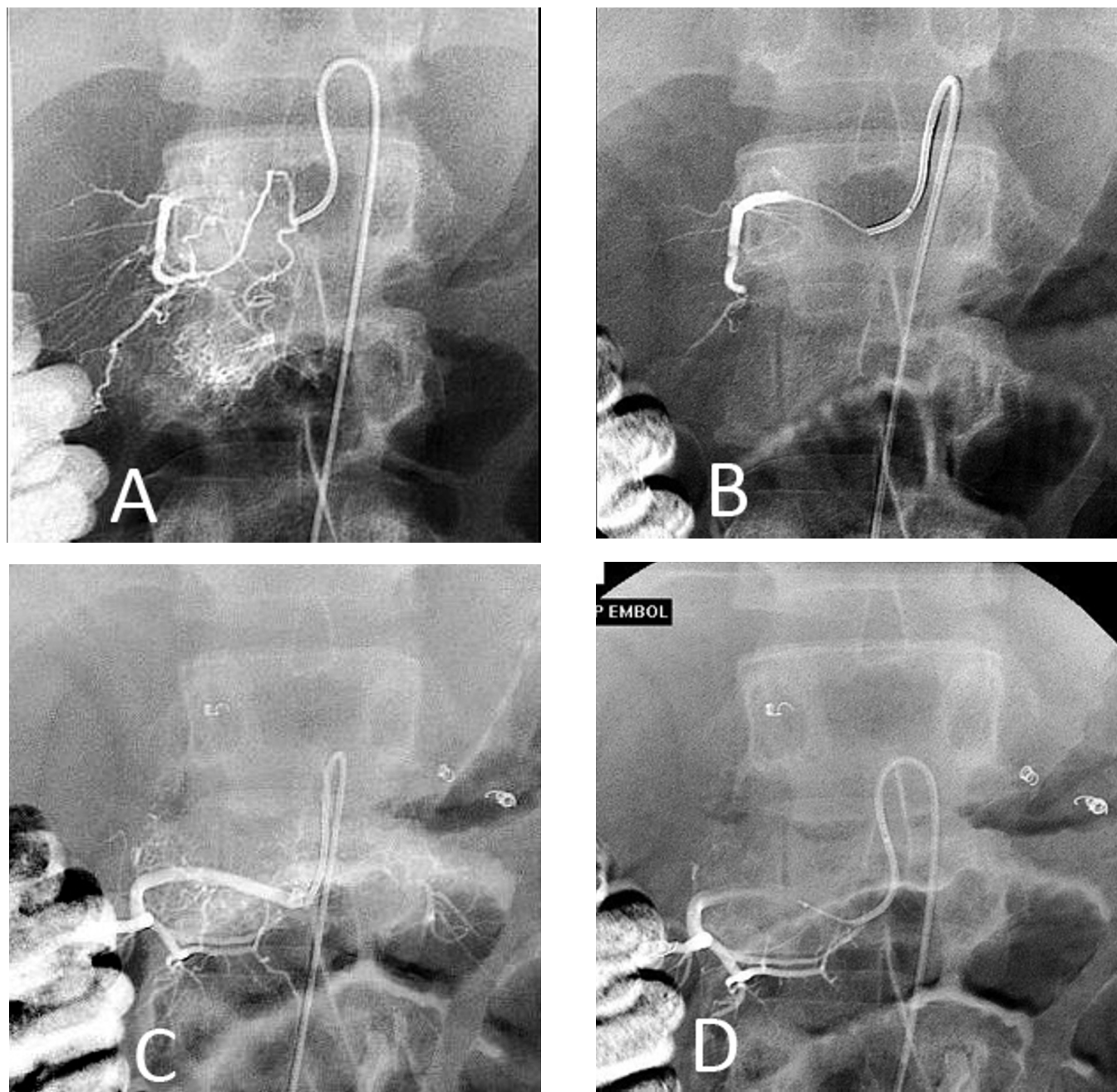


Figure 4. 27-year-old man with MNPST. Representative runs from spinal angiogram. A. Right L1 injection shows a hypervascular mass centered at the right side of the L2 vertebral body. B. Right L1 postembolization injection shows occlusion of the arterial feeders at that level. C. Right L2 injection shows that the hypervascular mass has multiple segmental and collateral feeders. Coils have already been placed at the L1 level on the right and the left. D. Right L2 postembolization injection shows successful occlusion of numerous arterial feeders supplying the tumor.

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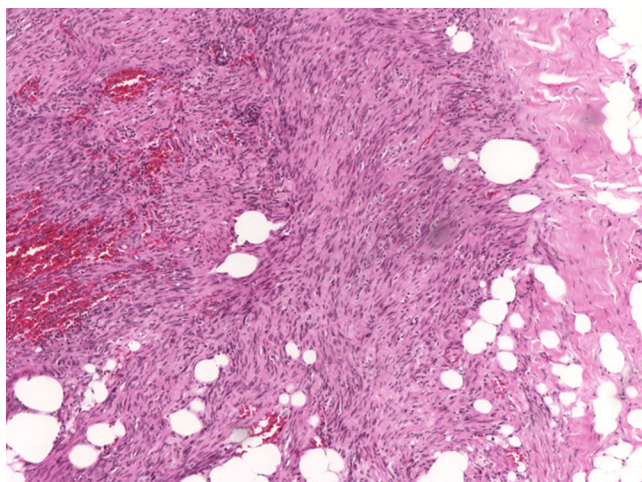


Figure 5. 27-year-old man with MPNST. Microscopic H & E-stained specimen shows neurofibromatous component of MPNST. There are interlacing wavy bands of collagen, associated with spindled cells with wavy nuclei and no significant pleomorphism.

tain bundles of elongated cells with wavy, dark-staining nuclei, associated with varying amounts of collagen fibrils and mucoid material (3, 6).

One of the signature imaging features of peripheral nerve sheath tumors is the MRI target sign (6-9), which appears as a central region of low signal intensity surrounded by high signal intensity on axial T2-weighted images. This target appearance likely reflects the underlying zonal architecture. In the case presented here, the MRI target sign is visible in a focal portion of the lesion located within the right L1-L2 neuroforamen (arrow in Fig. 3E). The corresponding region on CT also has a target appearance, with a central focus of high attenuation surrounded by an area of low attenuation (Fig. 2C). Since previous studies assert that the target sign is more common in benign as compared to malignant PNSTs (8-10), we speculate that the target sign in this case corresponds to the neurofibromatous portion of the lesion.

Malignant peripheral nerve sheath tumors

MPNSTs are aggressive soft-tissue sarcomas arising within peripheral nerve. Formerly referred to as malignant

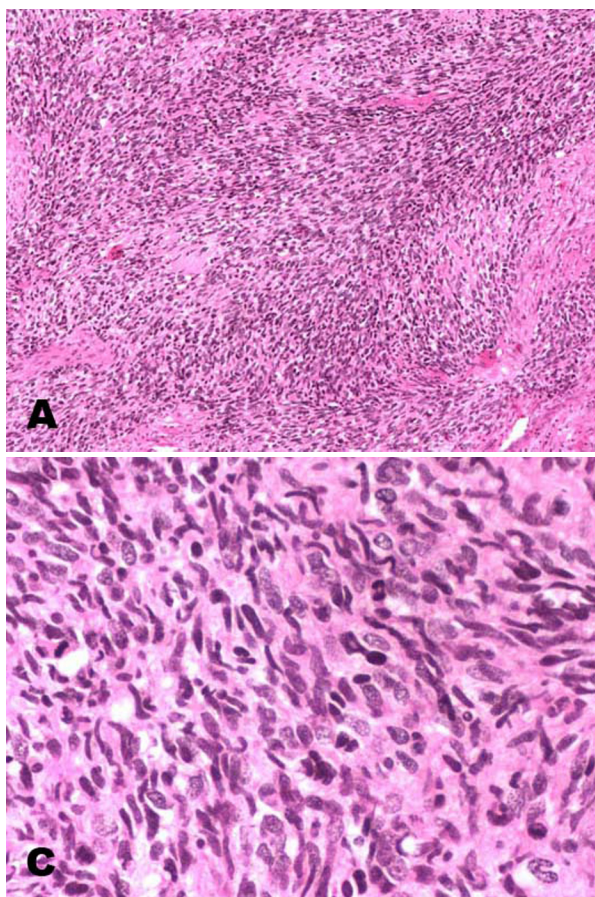


Figure 6. 27-year-old man with MPNST. Microscopic H & E-stained specimens of MPNST at medium (A, B), high (C), and low (D) power show a hypercellular spindle-cell lesion with cells variably arranged in a herringbone and fascicular pattern. There is severe cytologic atypia and nuclear pleomorphism, with focally brisk mitotic activity. No necrosis is present.

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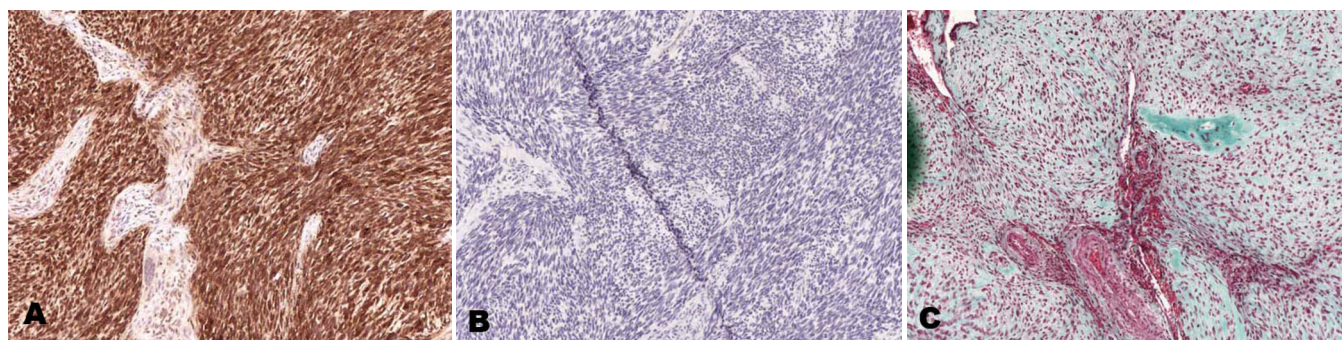


Figure 7. 27-year-old man with MPNST. Immunohistochemical examinations show diffuse positive immunostaining for p75 (A) and no significant immunostaining for C-kit (B). There are several foci of malignant osteoid on Gomori trichrome staining (C).

schwannomas, malignant neurilemmomas, neurogenic sarcomas, or neurofibrosarcomas, they account for up to 10% to 12% of soft-tissue sarcomas (3, 11). MPNSTs usually arise as a result of malignant transformation of neurofibromas in patients with NF1, or in sites of prior radiation therapy (1). MPNSTs are associated with NF1 in as many as 25% to 70% of cases (1-3, 12, 13), and NF1 patients have a lifetime risk of 8% to 13 % for developing a MPNST (14). Malignant degeneration from a sporadic neurofibroma however, as reported here, is uncommon and poorly described in the literature. Here we describe the imaging and histopathologic findings of a case of malignant degeneration of a benign lumbar spinal neurofibroma arising sporadically in a patient without underlying NF1.

Tissue diagnosis of MPNST is sometimes confounded by histologic similarity to other types of spindle-cell sarcomas, as well as by the variable presence of foci of divergent differentiation, including mesenchymal or epithelial elements (1, 11). The diagnosis in this case was challenging because of the unusual finding of malignant osteoid formation (Fig. 7C), as well as by the finding of bony invasion, which is somewhat atypical for MPNST (15). Outside histopathologic consultation was therefore obtained, and a provisional diagnosis of high-grade fibroblastic osteosarcoma was made. However, the results of specialized immunohistochemical stains, which showed p-75 immunopositivity and C-kit negativity (Fig. 7A,B), supported the diagnosis of MPNST. The final diagnosis was therefore not changed as a result of the outside consultation.

Treatment for MPNST is wide surgical excision, often followed by adjuvant chemoradiation. Despite aggressive treatment, prognosis remains poor, with a high rate of local recurrence and metastatic spread to lung, soft tissues, bone, liver, and other sites (1). It has been suggested that outcome is more favorable in sporadic cases. One study reports a five-year survival rate of 42% in sporadic cases, compared to 21% in NF1-associated MPNST (14). Since tumor size and extent of resection are likely to influence outcome (1), presurgical embolization is typically performed in cases of hypervascular spinal tumors. This not only limits operative blood loss but also improves the chances of complete tumor resection (16).

List of "red flags" for complicated low back pain (from Bradley 2007)

- Recent significant trauma, or milder trauma, with age over 50
- Unexplained weight loss
- Unexplained fever
- Immunosuppression
- History of cancer
- IV drug use
- Prolonged use of corticosteroids, osteoporosis
- Age over 70
- Focal neurologic deficit progressive or disabling symptoms
- Duration greater than 6 weeks

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